

The book does not include an author index. References pertaining to each chapter are summarized at the end of the book. These references are mostly to the Russian literature. Although the present treatise is based on lectures given by the author at the Lenin State University, it cannot be recommended by the reviewer as a university textbook; this book might, however, be of value to those who are interested in the Russian contribution to the science of catalysis.

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HERMAN PINES

Rates and Equilibria of Organic Reactions, As Treated by Statistical, Thermodynamic and Extrathermodynamic Methods.

By JOHN E. LEFFLER, Florida State University, Tallahassee, Fla., and ERNEST GRUNWALD, Bell Telephone Laboratories, Inc., Murray Hill, N. J. John Wiley and Sons, Inc., 605 Third Avenue, New York 16, N. Y. 1963. 458 pp. 6 × 9.5 cm. Price, \$11.00.

Unifying concepts are the beginnings from which new physical laws are built. The "extrathermodynamic method" is a successful, approximate concept which correlates substituent effects, solvent effects, and enthalpy-entropy relationships for rates and equilibria. The concept employs the same philosophy as thermodynamics, that in the absence of complete, microscopic understanding of the behavior of a system of molecules, a study of what is known is better than no study at all.

Interesting and well printed, with few errors noted by this reviewer, the contribution of Leffler and Grunwald details the background for, then the theory of, the extrathermodynamic method they have worked out. Along with their discussion, the authors present a large volume of data about linear free-energy relationships of all kinds and linear enthalpy-entropy relationships (as well as some nonlinear relationships).

Statistical and thermodynamic theories of equilibria and rates are presented in the first five chapters. This part of the book includes a nice introduction to the statistical thermodynamic method, a discussion of classical thermodynamics including a good explanation of standard states and activity coefficients, a very interesting discussion of reaction rates with some fine drawings of energy surfaces (but with an incomplete discussion of the origin of the transition-state rate equation), and a summary of fast equilibria in solution including experimental techniques, molecular collisions, and conformational equilibria.

Extrathermodynamic relationships are discussed in the last five chapters. A theoretical introduction is followed by detailed consideration of substituent and medium effects on free energy, enthalpy and entropy changes, and finally mechanochemical phenomena. The concept of *interaction mechanisms* between substituents provides a semiquantitative foundation for the discussion.

Naturally, any book has some shortcomings. This book tends to treat extrathermodynamic relationships as ends in themselves and purposely avoids much attempt at molecular interpretation.

The book is recommended to physical organic chemists for its unifying discussion, extensive data, and thought-provoking outlook.

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EDWARD R. THORNTON

Magnetism and the Chemical Bond. By JOHN B. GOODENOUGH, Lincoln Laboratory, Massachusetts Institute of Technology, Cambridge, Mass. John Wiley and Sons, Inc., Interscience Division, 605 Third Avenue, New York 16, N. Y. 1963. 393 pp. 16 × 24 cm. Price, \$12.50.

The average reader of this journal may well pick up Dr. Goodenough's book with a cry of joyous anticipation. He may soon put it down with a cry of dismay. But the fault is the author's only insofar as the title may be somewhat misleading. The real difficulty is that the average reader is not yet ready for this book. The book is a notable contribution to valence bond theory—even though it is restricted to "the origins of atomic moments and to magnetic ordering in solids." The author expresses the opinion that "an understanding of these two things should provide important foundation stones on which a theoretical superstructure for inorganic chemistry can be built. . . ." Certainly such a development is much to be desired, and certainly when that day comes Dr. Goodenough's book will be found to have helped.

The book is concerned with the magnitudes of the individual atomic, or ionic, magnetic moments, and the cooperative couplings between them. Here is a list of section headings: Description of the Free Atom, Molecules vs. Solids, Magnetism and the Chemical Bond, Ferromagnetism, Antiferromagnetism, Ferrimagnetism, Parasitic Ferromagnetism, Noncollinear Configurations, Neutron Diffraction Data, Atomic Moments and Their Interactions, Insulators and Semiconductors, Ionic Compounds with Metallic Conductivity, and Metals and Alloys. The formula index has over 500 entries. The level of presentation is about as advanced as possible at the present state of knowledge. The book is an intellectual feast, full of rich fare.

Chemists have long considered magnetism and the chemical bond to be one of their private domains. After all, the first relation of the two was developed by a great chemist, G. N. Lewis, and the first experimental proof of his ideas was published in the *Journal of the American Chemical Society*. But if chemists have made important contributions to the area, precious few of them are mentioned in the (extensive) bibliography of Dr. Goodenough's book. Among the people *not* mentioned are (besides Lewis): Orgel, Pacault, E. Müller, Klemm, Michaelis, and the Royal Dutch Shell Group in Amsterdam. Pauling and Nyholm rate one mention each. Any reader of this book would certainly gain the impression that magnetism and the chemical bond is an area in which no chemist has made a contribution worth more than passing mention. We all know that this is not true, yet the fact remains that the more searching recent studies on inorganic solids have all been made by physicists, and that solid state physics is today the most active branch of inorganic chemistry. Let us hope that chemistry is never reduced to snatching crumbs tossed them by the physicists, but rather that the new discipline of solid state chemical physics will grow as a natural and fruitful result of cooperative effort on the parts of both chemistry and physics. This means that both chemists and physicists should have an even better understanding of each other's methods and limitations, and, for the chemists it means an opportunity to obtain a much more complete foundation in mathematics and in atomic and molecular structure than many present curricula permit.

The book is a model of effective presentation. Errors are few and trivial, and the typography is well up to Interscience standards. One can hardly escape the feeling that in this book there will be found many a key to elusive problems in many areas of inorganic chemistry. And many a reader will see for himself how far from reality are most elementary presentations of both magnetism and of valence bond theory.

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Grundlagen der Arzneimittelforschung und der synthetischen Arzneimittel.

By DR. JAKOB BÜCHI, Professor für Pharmazeutische Chemie an der Eidg., Techn. Hochschule Zürich; Direktor des Pharmazeutischen Instituts. Birkhäuser Verlag, Basel 10, Switzerland. 1963. 744 pp. 17 × 25 cm. Price, sFR. 96.

Any author who ventures to write a book entitled "The Principles of Drug Research and Synthetic Drugs" has set himself a formidable task. Many an intrepid explorer has searched the Seven Seas for the mysterious philosopher's stone of the 20th century, the Secret (punch card) Codex that gives the chemical structure required for any desired biological activity. He sets foot in the land of Natural Products, only to be told that the secret lies on the nearby islands inhabited by the Organic Chemists. From there he is sent to visit their relatives, the Physical Chemists, the Pharmaceutical Chemists, the Analytical Chemists, and their cousins the Biochemists. None have the Secret Codex, although each in his own language is able to quote from it at some length. He travels further, and comes upon other tribes: the Bacteriologists, the Chemical Pathologists, the Pharmacologists, the Endocrinologists, and the Clinicians—each (in his different language) claims to have the Codex, but has in fact only part of it. Finally our explorer, older, sadder, and wiser, returns and realizes that it is only the sum of the individual contributions that together make up the document.

The author has admirably recognized this truth, and while many monographs exist which deal with highly specialized sections of drug action, he has endeavored to present a comprehensive panoramic view of the whole field of the present status of drug research, and has by this means made a valuable addition to the literature of the subject.

The book is divided into six chapters. An introductory chapter traces the many disciplines that take part in the creation and evaluation of a new drug, and the closely integrated teamwork which this requires. Gone are the days when a lone scientist, working in his attic through the vigils of the night, could discover a sensational new drug. The author points out that, because of the large teams involved, the development of new drugs has today become almost totally the province of the phar-

maceutical industry. Nevertheless, academic researchers can make powerful contributions by concerning themselves with specific problems of *fundamental research*, such as the isolation and structure determination of natural products, the discovery of new synthetic methods, and the mechanism of action of specific drugs.

He distinguishes very clearly between the mere preparation of just another compound (which brings no progress and possesses no clear advantage over a known drug except that it is a different compound) on the one hand, and the development of a more efficacious drug (resulting in a lower dose, reduced side effects, lower toxicity, improved stability, etc.) as an indication of real progress, on the other hand.

After a historical summary of the empirical discovery of most drugs, the author concludes that the planned design of new drugs is still comparable to shooting at a target in the dark. A great deal more investigation of mechanism and mode of action is needed before our knowledge of the interaction between drug and receptor site will make it possible to "design" a drug for a specific function.

Chapter 2 (the longest) reviews the several different fields and aims of drug research: The isolation of natural products, purification of active components, chemical synthesis, and chemical modification of known structures by all available methods, are dealt with by means of a wealth of examples, lavishly illustrated with structural formulas, tables, and diagrams. Attention is then turned to the physical organic techniques now available, and their application to gain valuable insights into the steric arrangements of many biologically active, cyclic molecules, and their interaction with possible receptor sites. The phenomena of bio-isosterism, of vinylogy, and of "pseudo-rings" are discussed, and the ways in which small chemical modifications affect the biological activity of many drugs are documented, with many examples. After a fundamental discussion of the necessary analytical-chemical measurements, there are sections on the principles of bacteriological and pharmacological testing, on drug formulation, and on clinical trials and their evaluation.

Chapter 3 is devoted to a discussion of the many physico-chemical properties which may affect pharmacological activity. The Ferguson principle is introduced, and surface effects considered. Chapter 4 lists the major biochemical modifications which occur in drug metabolism. Hydroxylation, oxidation, reduction, methylation and demethylation, and other detoxication mechanisms are presented.

The relationship between chemical constitution and pharmacological activity occupies Chapter 5 and is given in terms of modern concepts, utilizing *inter alia* aspects of configuration and conformation, the stereochemistry of optical isomers and their interaction with receptor sites, the influence of inductive and mesomeric effects, polarizable groups, and dipole moments.

It is clear that even with all presently available physical methods, valid prognostications in this field can only be made for compounds of closely similar chemical structures, possessing the same biological activity. However, recent progress in the understanding of modes of drug action is well summarized in Chapter 6. Here, such topics as drug-receptor theory, enzyme inhibition, antimetabolite action, and the function of chelation are discussed and illustrated with numerous diagrams. The author rightly emphasizes the fundamental importance of gaining further insight into the mode of action of drugs by the use of all newly available techniques, and stresses especially the role of the organic and physical organic chemist in this monumental task. Only through a more exact knowledge of the conformation and reactivity of active compounds can more detailed knowledge of the architecture of the biological receptor site be gained.

The book is well written and makes interesting reading. Ample references (a total of more than 1600) to the original literature (in many cases up to 1962) are cited. The printing and binding are of excellent quality. There are a few minor typographical errors (this reviewer found only six).

In any work of this magnitude, it is inevitable that a few inaccuracies will occur: morphine-N-oxide in fact possesses very little analgetic activity (p. 69); metabolites of nicotine other than nicotinic acid *have* been isolated (p. 485); many metabolites of chlorpromazine, other than the sulfoxide, are now known (p. 485); the methylolamine derivative from 4-dimethylaminoazobenzene has *not* in fact been obtained (p. 501); the mode of action of isonicotinic hydrazide has been shown *not* to involve the inhibition of transaminase by the compound formed with pyridoxal (p. 695). However, these minor criticisms do not seriously detract from the value of the book for the purpose stated by the author. It is attractively presented and is recommended to all those who have interests in the field of chemical-biological correlation.

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